

Patent claims as attached to the IPER

1. Flow-through shear analyser for measuring the
adsorption-desorption and reaction kinetics of molecules with
5 signal-generating properties on surfaces, comprising
a sample chamber block

with a sample chamber located therein for receiving
analysis or buffer solution, which sample chamber
comprises at least one sample chamber wall made of
10 a radiation-permeable material;
with a supply line for the buffer solution into the
sample chamber and a removal line for the buffer
solution out of the sample chamber; and with a
closable injection opening on the supply line-side
15 of the sample chamber for introducing a sample
solution;

a means for generating extremely thin liquid layers in
the buffer solution located in the sample chamber, so that
the adsorption rate of the signal-generating molecules on the
20 measurement surface is not influenced by the mass transport
of the molecules to this interface layer between solution and
surface;

an analyser unit for direction and evaluation of the
signals emitted by the signal-generating molecules, or of the
25 influence of the physical and optical parameters of the
measurement surface as determined by the molecules by
changing the measurable surface signals or surface radiation
emerging from the surface; composed of

if required, a radiation source, at least one radiation
30 conduit and a radiation analyser;

a pump for supplying of the chamber solution via the
supply line in the sample chamber; and, as the case may be,
a pump for removal of the chamber solution from the
sample chamber via the removal line,

35 wherein the means for generating extremely thin liquid
layers are formed as an apparatus arranged on the supply
line-side, which apparatus subdivides the volume flow of the
chamber solution in the supply line by introduction of at

least one volume unit of the fluid which is immiscible in the chamber solution, if desired by subjecting to pressure.

2. The analyser according to claim 1, characterized in
5 that the chamber solution is composed of a hydrophilic (polar) or hydrophobic (non-polar) liquid.

3. The analyser according to claim 1-2, characterized in
10 that the fluid which is immiscible with the respective chamber solution is composed of gas or of a liquid which is immiscible with the chamber liquid.

4. The claim according to 1-3, characterized in that the
15 chamber solution is composed of a buffer and the immiscible fluid is composed of air.

5. The analyser according to claim 1-4, characterized in
20 that the sample chamber for receiving analysis or buffer solution is outfitted as a radiation-permeable flow-through cuvette with a rectangular or circular cross section perpendicular to the direction of flow.

6. The analyser according to claim 1-5, characterized in
25 that the radiation analysis unit is composed of a light source which delivers a monochromatic light beam, a radiation conduit, preferably an optical prism and a radiation analyser, preferably an emission monochromometer with an evaluation unit connected thereto, wherein the radiation
30 conduit and the light source are arranged with respect to one another such that the light beam emerging from the light source impinges upon the interface layer between the sample chamber wall and the solution via the radiation conduit arranged in an optically coupled fashion on the radiation-permeable sample chamber wall at an angle which is larger
35 than the critical angle for the more dense medium, and the fluorescence light formed, which fluorescence light is generated at the interface layer between the sample chamber wall and the sample liquid in the sample chamber, and which

emerges essentially perpendicular to the surface of the sample chamber wall, is directed via an optical system into the radiation analyser.

5 7. The analyser according to claim 6, characterized in that the sample chamber wall is composed of a radiation-permeable material made of quartz glass, preferably in the form of a quartz glass plate.

10 8. The analyser according to claim 6 or 7, characterized in that the radiation conduit is a prism or a glass fiber lead.

15 9. The analyser according to claim 6, 7 or 8, characterized in that the radiation analyser is an emission monochromometer.

20 10. A method according to claim 1-9, characterized in that the signal generating molecules are biologically active molecules.

25 11. The method according to claim 1-10, characterized in that the signal generating biologically active molecules are proteins which are capable of radiation, and which can react with ligands.

30 12. The analyser according to one of claims 1-11, characterized in that the side of the sample chamber wall made of a radiation-permeable material, which side of the sample chamber wall is directed towards the inside of the sample chamber, is provided with a coating which promotes the coupling or the binding of the radiation-capable molecules, which coating can act in a specifying manner.

35 13. Flow-through shear analyser for measuring the adsorption-desorption and reaction kinetics of molecules with signal-generating properties on surfaces, comprising a sample chamber block

with a sample chamber located therein for receiving analysis or buffer solution, which sample chamber comprises at least one sample chamber wall made of a radiation-permeable material;

5 with a supply line for the buffer solution into the sample chamber and a removal line for the buffer solution out of the sample chamber; and with a closable injection opening on the supply line-side of the sample chamber for introducing a sample
10 solution;

a means for generating extremely thin liquid layers in the buffer solution located in the sample chamber, so that the adsorption rate of the signal-generating molecules on the measurement surface is not influenced by the mass transport
15 of the molecules to this interface layer between solution and surface;

an analyser unit for direction and evaluation of the signals emitted by the signal-generating molecules, or of the influence of the physical and optical parameters of the
20 measurement surface as determined by the molecules by changing the measurable surface signals or surface radiation emerging from the surface; composed of

if required, a radiation source, at least one radiation conduit and a radiation analyser;

25 a pump for supplying of the chamber solution via the supply line in the sample chamber; and, as the case may be,

a pump for removal of the chamber solution from the sample chamber via the removal line,

wherein the means for generating the extremely thin
30 liquid layers are formed in that the sample chamber is formed as a cylindrical rheometer chamber for receiving analysis or sample buffer,

its one end is tightly closed by a light-permeable quartz plate,

35 in which a cylindrical rotor made of a light-permeable material is rotatably mounted, the outer diameter of which is adapted to the inner diameter of the rheometer chamber, wherein the cylindrical rotor is formed to be conical on the

side facing the quartz plate and touches the quartz plate with the cone point laying in the rotational axis of the rotor; and

which comprises a supply line and a removal line for the buffer solution into the sample chamber, itself formed by rheometer chamber inner walls, a rotor cone and a light-permeable quartz plate; and

a motor for driving the rotor is provided.

14. The analyser according to claim 13, characterized in that the supply line and the removal line of the sample solution are arranged essentially diametrical to the rotational axis of the rotor.

15. The analyser according to claims 13 or 14, characterized in that the supply line and the removal line are arranged in the light-permeable quartz plate.

16. The analyser according to claim 15, characterized in that the supply line is arranged on the light-permeable quartz plate close to the rotational axis of the rotor and the removal line is arranged on the light-permeable quartz plate at the outer border of the sample chamber in line with the rotational axis of the rotor.

17. The analyser according to one of the previous claims, characterized in that the closable injection opening for introducing a sample solution into the sample chamber is arranged in the supply line.

18. The analyser according to one of the claims 12-17, characterized in that the angle between the rotor axis and the tangential on the cone surface is 85° - 89.9° .

19. The analyser according to one of the claims 12-18, characterized in that further means for generating extremely thin liquid layers are provided in the form of an apparatus arranged on the supply line-side, wherein this apparatus sub-

divides the volume flow of the buffer solution in the supply line by introducing volume units of a fluid which is immiscible in the buffer solution.

5 20. The analyser according to claim 19, characterized in that the fluid which is immiscible in the buffer solution is composed of gas or a liquid which is immiscible in the buffer solution.

10 21. A method for determining the thickness of an ultra-thin liquid layer, characterized in that an ultra-thin liquid layer is generated on the measurement surface by feeding an immiscible fluid into the liquid flow of a strongly
15 fluorescing fluorophore which does not adsorb at the solid/liquid interface, and an evanescent light wave of high penetration depth is radiated through this ultra-thin liquid layer to such an extent that a measurement signal, for
20 example a measurable reduction of the fluorescence signal, is evolved by the entry of the evanescent wave into the inside of the non-fluorescing fluid.

22. A method for the analysis of a liquid for a component present in the liquid in a sample analysis chamber, characterized in that the liquid flow to be fed through the
25 sample analysis chamber is subdivided into volume flow segments in the supply line prior to entry into the sample analysis chamber by a fluid which is not miscible in the liquid, the segmented volume flow segments are subsequently directed into the sample analysis chamber, and then the
30 volume flow segments in the analysis chamber are investigated for the component enriched at the interface layer between the solid phase/liquid or between the fluid/liquid.

23. A method for the analysis of a liquid for a
35 component present in the liquid in a sample chamber, characterized in that the liquid flow to be directed through the sample analysis chamber is subdivided into volume flow segments in the supply line prior to introduction into the

sample analysis chamber by a fluid which is immiscible in the liquid, subsequently directing the segmented volume flow segments into the sample analysis chamber and then investigating the volume flow segments in the analysis chamber for the component enriched in the bulk of the immiscible fluid.

24. The method according to claim 21 or 22, characterized in that the fluid which is immiscible in the liquid of the liquid flow is composed of gas or an immiscible liquid.

25. The method according to one of claims 22-24, characterized in that the liquid flow is directed in the direction of the sample analysis chamber via a two-way valve with one supply line each for the liquid flow and the fluid which is immiscible in the buffer solution and a common removal line, wherein during analysis of the liquid flow in the sample analysis chamber intermittent switching between the two sample line positions in the two-way valve takes place.

26. The method according to one of claims 21-25, characterized in that the shearing force-engendering liquid flow which moves the ultra-thin liquid layer generated with the help of the fluid on the surface in the flow direction, is stopped for the measurement of the component present in the liquid or for the determination of the layer thickness of the liquid layer.

27. The method according to one of claims 21-26, characterized in that the liquid flow is reversed in its direction for the measurement of the component present in the liquid or of the layer thickness.

28. The method according to claim 21-27, characterized in that the temperature for the measurement of the component present in the liquid is changed in a jumpwise fashion.

29. A method for the determination of adsorption-,
desorption- or reaction rate constants of signal-generating
molecules on surfaces using the analyser according to one of
5 the claims 1 to 20, which method comprises the following
steps:

Directing a buffer solution through the sample chamber
in the analyser;

10 Introducing the sample solution to be studied via the
injection opening in the sample chamber;

Irradiating the optical prism with monochromatic light
at a critical angle of about 70° ;

15 Measuring the light intensity of the fluorescent light
which is generated at the interface layer between the quartz
plate and the sample chamber, and which exits essentially
perpendicular to the quartz plate and enters essentially
perpendicular into the emission monochrometer.

20 30. The method according to claim 30, characterized in
that prior to the introduction of the sample solution into
the sample chamber a fluid which is immiscible in the sample
solution is introduced into the supply line in a volume of
maximum 1000 μl .

25 31. The method according to claim 29 or 30,
characterized in that the fluid is introduced into the sample
chamber in the form of an air bubble.